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published in

British Journal of Psychiatry
2012

DOI (link to publisher)

[10.1192/bjp.bp.111.097550](https://doi.org/10.1192/bjp.bp.111.097550)

document version

Publisher's PDF, also known as Version of record

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citation for published version (APA)

Boschloo, L., Vogelzangs, N., van den Brink, W., Smit, J. H., Veltman, D. J., Beekman, A. T. F., & Penninx, B. W. J. H. (2012). Alcohol use disorders and the course of depressive and anxiety disorders. *British Journal of Psychiatry*, 200(6), 476-484. <https://doi.org/10.1192/bjp.bp.111.097550>

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The British Journal of Psychiatry

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BJP 2012, 200:476-484.

Access the most recent version at DOI: [10.1192/bjp.bp.111.097550](https://doi.org/10.1192/bjp.bp.111.097550)

References

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Alcohol use disorders and the course of depressive and anxiety disorders

Lynn Boschloo, Nicole Vogelzangs, Wim van den Brink, Johannes H. Smit, Dick J. Veltman, Aartjan T. F. Beekman and Brenda W. J. H. Penninx

Background

Inconsistent findings have been reported on the role of comorbid alcohol use disorders as risk factors for a persistent course of depressive and anxiety disorders.

Aims

To determine whether the course of depressive and/or anxiety disorders is conditional on the type (abuse or dependence) or severity of comorbid alcohol use disorders.

Method

In a large sample of participants with current depression and/or anxiety ($n = 1369$) we examined whether the presence and severity of DSM-IV alcohol abuse or alcohol dependence predicted the 2-year course of depressive and/or anxiety disorders.

Results

The persistence of depressive and/or anxiety disorders at the 2-year follow-up was significantly higher in those with

remitted or current alcohol dependence (persistence 62% and 67% respectively), but not in those with remitted or current alcohol abuse (persistence 51% and 46% respectively), compared with no lifetime alcohol use disorder (persistence 53%). Severe (meeting six or seven diagnostic criteria) but not moderate (meeting three to five criteria) current dependence was a significant predictor as 95% of those in the former group still had a depressive and/or anxiety disorder at follow-up. This association remained significant after adjustment for severity of depression and anxiety, psychosocial factors and treatment factors.

Conclusions

Alcohol dependence, especially severe current dependence, is a risk factor for an unfavourable course of depressive and/or anxiety disorders, whereas alcohol abuse is not.

Declaration of interest

None.

Depressive and anxiety disorders are highly prevalent in the general population,¹ and have an enormous impact on physical, social and occupational functioning.^{2–6} These severe impairments may be long-lasting because depressive and anxiety disorders frequently have a persistent course.^{7–11} Identification of risk factors that predict unfavourable outcomes may provide important insights into processes involved in the natural course of these disorders and is essential for optimising treatment strategies. Alcohol use disorders (abuse and dependence) are highly prevalent in people with depression and/or anxiety,^{12–15} and have been suggested to be important predictors of a poor outcome. However, few prospective studies have examined the effects of alcohol use disorders on the natural course of depressive and anxiety disorders, and these have reported conflicting results. For example, people with comorbid alcoholism have a decreased risk of remission of major depressive disorder,¹⁶ and in addition remission of generalised anxiety disorder is less likely in people with comorbid substance use disorders.¹⁷ However, other studies failed to find alcohol use disorders to be significant predictors of the persistence of disorder among people who had depression or anxiety.^{11,18} These inconsistent findings may be partly explained by these studies' lack of power owing to small sample sizes ($n = 588$, $n = 473$, $n = 400$ and $n = 92$ respectively).^{11,16–18} Therefore, we prospectively examined the 2-year course of depressive and/or anxiety disorders in a large sample of participants with current depression and/or anxiety ($n = 1369$).

Another possible explanation for the inconsistent results is the heterogeneity of alcohol use disorders. Previous studies have shown that alcohol dependence has strong cross-sectional associations with depressive and/or anxiety disorders, whereas alcohol abuse has not.^{14,15} It may, therefore, be important to examine the unique associations of each condition on the natural course of depressive and anxiety disorders. In addition, it may be

necessary to take into account the severity of alcohol abuse and dependence, since these conditions have a dimensional aspect.^{19–21} Consequently, our study not only examined whether the presence of an alcohol use disorder predicts the course of depressive and/or anxiety disorders, but also explored whether this association is conditional on the type of alcohol use disorder (abuse or dependence) or the severity of each condition. In addition, we examined whether found associations might be due to or independent of baseline severity of depressive and/or anxiety disorders, and of psychosocial and treatment factors.

Method

Study sample

Data were derived from the Netherlands Study of Depression and Anxiety (NESDA), an ongoing cohort study aimed at examining the long-term course and consequences of depressive and anxiety disorders in the adult population (aged 18–65 years). A total of 2981 persons were included at the baseline assessment in 2004–7, consisting of a healthy control group, people with a history of depressive or anxiety disorder and people with current depressive and/or anxiety disorder. Participants were recruited from community (19%), primary care (54%) and out-patient mental healthcare services (27%). Community-based participants had previously been identified in a population-based study. Primary care participants were identified through a three-stage screening procedure, involving the 10-item Kessler questionnaire and the Short Form Composite International Diagnostic Interview (CIDI),^{22,23} conducted by telephone among a random sample of patients of 65 general practitioners. Mental healthcare participants were recruited consecutively when newly enrolled at one of the 17 participating mental health organisation locations. People with

insufficient command of the Dutch language or a primary clinical diagnosis of bipolar disorder, obsessive-compulsive disorder, severe substance use disorder, psychotic disorder or organic psychiatric disorder, as reported by them or their mental health practitioner, were excluded. The research protocol was approved by the ethical committee of participating universities and all participants provided written informed consent. A detailed description of the NESDA study design, sampling procedures and response rates can be found elsewhere.^{24,25} In our earlier research we examined non-response at the baseline interview: in participants recruited from primary care (the majority), mainly sociodemographic factors – namely younger age and male gender – but not mental health status predicted higher non-response.²⁵ Similar observations were found in the community and mental healthcare settings.²⁴ This suggests that our overall sample is generalisable to the sample from which it was recruited, although younger men may be slightly underrepresented.

The baseline assessment included a face-to-face assessment of demographic and personal characteristics as well as a standardised diagnostic psychiatric interview among all 2981 NESDA participants. After 2 years, another face-to-face assessment including the same standardised diagnostic psychiatric interview was conducted, with a response of 87.1% ($n = 2596$; see Lamers *et al* also for sociodemographic and psychiatric determinants of non-response).²⁶ For this study we selected all participants with major depressive disorder, dysthymia, social phobia, panic disorder and/or generalised anxiety disorder that was present within the 6 months prior to the baseline assessment ($n = 1641$). Of these, 1369 persons (83.4%) had complete data at the 2-year follow-up assessment and formed the sample for the analyses presented here. The non-response group was significantly younger ($P = 0.03$), less educated ($P < 0.001$) and more often had a current depressive disorder ($P = 0.003$) at baseline compared with the responder group, whereas gender ($P = 0.16$), alcohol abuse/dependence status ($P = 0.74$) and current anxiety disorder ($P = 0.07$) were not associated with failure to respond.

Measures

Depressive and anxiety disorders

Diagnoses of psychiatric disorders according to DSM-IV criteria²⁷ were established with the CIDI version 2.1, administered by specially trained research staff.²³ The CIDI has shown high interrater and test–retest reliability and high validity for depressive and anxiety disorders.²³ To examine the course of depressive and/or anxiety disorders, we considered the persistence of the disorder as well as the course of symptoms.

Persistence. Participants were considered to have persistent disorder if they met DSM-IV criteria for a depressive and/or anxiety disorder in the 6 months prior to the 2-year follow-up assessment.

Symptoms. To assess the robustness of findings regarding the persistence of these disorders, the course of symptoms during the 2-year follow-up was used as a secondary outcome. Depressive symptoms were defined as the total score on the 30-item self-report Inventory of Depressive Symptomatology (IDS);²⁸ anxiety symptoms were defined as the total score on the 21-item self-report Beck Anxiety Inventory (BAI).²⁹ Both questionnaires related to symptoms in the week prior to assessment. In addition to the baseline and 2-year follow-up interviews, the IDS and BAI were also administered at an intermittent 1-year follow-up assessment.

Alcohol use disorder

Diagnoses of alcohol use disorder (DSM-IV criteria) were established at baseline with the CIDI, which is a reliable and valid instrument for assessing alcohol dependence, but with more variable results for alcohol abuse.³⁰ A DSM-IV diagnosis of alcohol abuse requires one or more of the four abuse criteria to be met, whereas a diagnosis of alcohol dependence requires three or more of the seven dependence criteria. The CIDI hierarchy criteria for diagnosing DSM-IV alcohol use disorders exclude the possibility of a diagnosis of alcohol abuse when a lifetime diagnosis of alcohol dependence is present. A distinction was made between alcohol use disorders that were present in the 6 months prior to the baseline assessment (current disorder) *v.* before this period (remitted disorder). Various alcohol use disorder measures were assessed to examine the exact effects of this disorder on the course of depressive and/or anxiety disorders.

Alcohol use disorder status. Alcohol use disorder status – no lifetime alcohol use disorder (reference category), remitted disorder or current disorder – was used to examine whether these categories predicted the course of depressive and/or anxiety disorders.

Alcohol abuse/dependence status. To determine whether DSM-IV alcohol abuse and dependence have differential effects on the course of depressive and/or anxiety disorders, we distinguished between participants with no lifetime alcohol use disorder (reference category), remitted alcohol abuse, current abuse, remitted dependence and current dependence.

Alcohol abuse/dependence severity. The severity of current alcohol abuse and dependence diagnoses was defined by the number of criteria met, *i.e.* one to four criteria for alcohol abuse and three to seven criteria for dependence. Previous studies have shown that alcohol abuse and dependence have a dimensional aspect,^{19,20} and that the count of alcohol dependence criteria constitutes a linear dimension of alcohol dependence severity.²¹

Covariates

Basic covariates comprised gender, age (in years) and smoking status (never smoked, former smoker, current smoker) at baseline. To examine the role of baseline severity of depressive and/or anxiety disorders, psychosocial factors and treatment factors in the association between alcohol use disorders and the course of depressive and/or anxiety disorders, analyses were additionally adjusted for the following covariates.

Severity of depression and anxiety

Severity of depression and anxiety was defined as the severity of symptoms at baseline assessed with the IDS and BAI respectively.

Psychosocial factors

Psychosocial factors included education (in years), employment status (no/yes) and partner status (no/yes) at the baseline assessment.

Treatment factors

Treatment factors consisted of frequent use of antidepressants, frequent use of benzodiazepines and psychological treatment at the baseline interview and/or during follow-up. Frequent use of psychoactive medication was assessed by drug container inspection of medication used in the month before the baseline

or 2-year follow-up assessment, classified according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification,³¹ and was considered to be present when the medication was taken daily or on at least half of the days. We distinguished between use of antidepressants – selective serotonin reuptake inhibitors (ATC code N06AB), tricyclic antidepressants (N06AA) and other antidepressants (N06AF/N06AX) – and use of benzodiazepines (ATC codes N03AE, N05BA, N05CD and N05CF). The receipt of psychological treatment (formal psychotherapy, counselling or skills training) in the 6 months prior to the baseline or 2-year follow-up assessment was based on self-reported information.

Statistical analysis

Analyses were conducted using SPSS version 15.0 for Windows. First, baseline characteristics of the sample were summarised using descriptive statistics. To examine whether alcohol use disorder status (no lifetime disorder, remitted disorder or current disorder) predicted the presence of depressive and/or anxiety disorders at the 2-year follow-up, logistic regression analyses were used. We then focused on the type of alcohol use disorder by examining the associations across alcohol abuse/dependence status: no lifetime alcohol use disorder (reference category), remitted alcohol abuse, current abuse, remitted dependence and current dependence.

We further explored the relationships of current alcohol abuse and dependence with the presence of depressive and/or anxiety disorders at the 2-year follow-up by focusing on the severity of the current alcohol use disorder. A graph was plotted based on logistic regression analyses with variables representing all separate levels of abuse severity (one to four criteria) or dependence severity (three to seven criteria) as predictors. We used the Wald statistic to test whether a model based on alcohol abuse or dependence severity better predicted the presence of depressive and/or anxiety disorders at 2-year follow-up than the model based on DSM-IV alcohol use disorder diagnoses, an analytic method used previously by others.²¹ All analyses were adjusted for gender, age and smoking status.

To test the robustness of our findings, we additionally examined the course of depressive symptoms as well as anxiety symptoms using linear mixed models (LMM) analyses. Alcohol abuse/dependence status, time of assessment (baseline, 1-year follow-up, 2-year follow-up) and covariates were entered as fixed factors, participants were treated as a random effect and a random intercept was estimated. To determine whether groups based on alcohol abuse/dependence status differed in their overall levels of depressive and anxiety symptoms, we considered the direct effects of alcohol use disorder groups. In addition, we added a group × time interaction term to examine whether the trajectories of depressive and anxiety symptoms differed across the groups. Similarly, we used LMM analyses to examine whether the alternative model based on abuse/dependence severity predicted the course of depressive and anxiety disorders. To examine the role of other factors in the association between alcohol use disorders and the persistence of depressive and/or anxiety disorders, analyses were additionally adjusted for covariates involving baseline severity of depression and anxiety (IDS and BAI total scores), psychosocial factors (education, employment status and partner status) and treatment factors (use of antidepressants, use of benzodiazepines and psychological treatment).

Results

Our sample (*n* = 1369) had a mean age of 41.3 years (*s.d.* = 12.3) and two-thirds (66.3%) were women; 935 persons (68.3%) had

never had an alcohol use disorder, 307 (22.4%) had a remitted alcohol use disorder and 127 (9.3%) had a current alcohol use disorder (Table 1).

Alcohol use disorder status

We examined whether alcohol use disorder status predicted the presence of depressive and/or anxiety disorders after 2-year follow-up, adjusted for basic covariates. Neither remitted nor current alcohol use disorder was a significant predictor of an unfavourable course of depressive disorder and/or anxiety disorder compared with those with no lifetime alcohol use disorder (Table 2).

Type of alcohol use disorder

We tested whether alcohol abuse and dependence had differential effects on the course of depressive and/or anxiety disorders, adjusted for basic covariates (Table 2). Participants with depression and/or anxiety with remitted alcohol dependence (persistence: 62.4%; odds ratio (OR) = 1.42, 95% CI 1.02–1.97, *P* = 0.04) and those with current alcohol dependence (persistence: 66.7%; OR = 1.69, 95% CI 1.04–2.75, *P* = 0.04) had a significantly

Table 1 Sample characteristics at baseline (*n* = 1369)

Basic covariates	
Gender, female, <i>n</i> (%)	907 (66.3)
Age, years: mean (<i>s.d.</i>)	41.3 (12.3)
Smoking, <i>n</i> (%)	
Non-smoker	363 (26.5)
Former smoker	430 (31.4)
Current smoker	576 (42.1)
Severity of depression and anxiety	
Depressive symptoms (IDS total score): mean (<i>s.d.</i>)	28.9 (12.2)
Anxiety symptoms (BAI total score): mean (<i>s.d.</i>)	16.7 (10.4)
Psychosocial factors	
Education, years: mean (<i>s.d.</i>)	11.9 (3.3)
Employment (yes), <i>n</i> (%)	758 (55.4)
Partner (yes), <i>n</i> (%)	890 (65.0)
Treatment, <i>n</i> (%)	
Use of antidepressants (yes)	632 (46.2)
Use of benzodiazepines (yes)	239 (17.5)
Psychological treatment (yes)	915 (66.8)
AUD measures, <i>n</i> (%)	
AUD status	
No lifetime AUD	935 (68.3)
Remitted AUD	307 (22.4)
Current AUD	127 (9.3)
AA/AD status	
No lifetime AUD	935 (68.3)
Remitted AA	113 (8.3)
Current AA	46 (3.4)
Remitted AD	194 (14.2)
Current AD	81 (5.9)
Number of current AA criteria, <i>n</i> (%)	
One	44 (3.2)
Two	2 (0.1)
Three	0 (0.0)
Four	0 (0.0)
Number of current AD criteria, <i>n</i> (%)	
Three	26 (1.9)
Four	22 (1.6)
Five	13 (0.9)
Six	12 (0.9)
Seven	8 (0.6)

AA, alcohol abuse; AD, alcohol dependence; AUD, alcohol use disorder; BAI, Beck Anxiety Inventory; IDS, Inventory of Depressive Symptomatology.

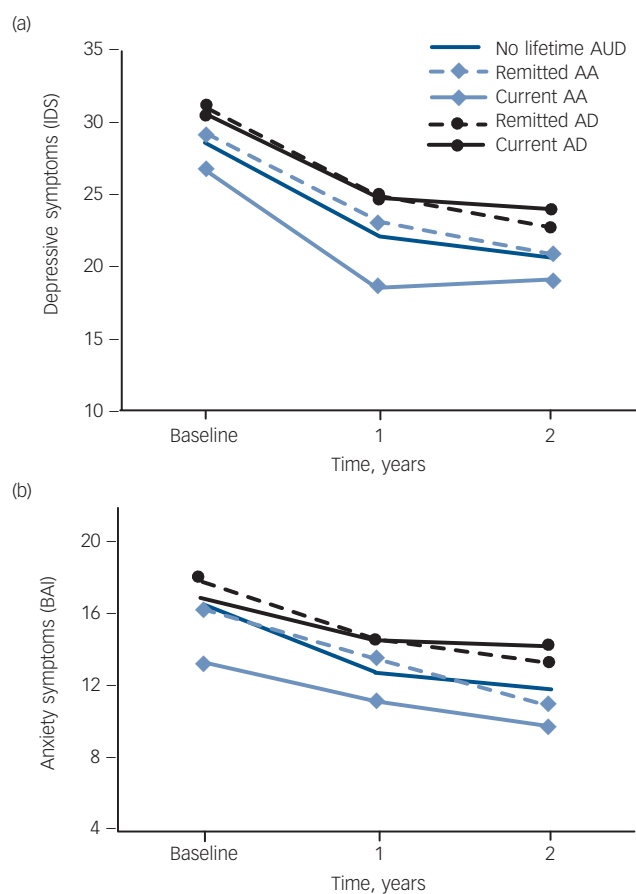
Table 2 Alcohol use disorder measures predicting the persistence of depressive and/or anxiety disorder at 2-year follow-up

Baseline AUD measure	Persistence of depressive/anxiety disorder		
	Rate, %	OR ^a (95% CI)	P
AUD status			
No lifetime AUD	53.2	Reference	
Remitted AUD	58.3	1.21 (0.92–1.60)	0.17
Current AUD	59.1	1.27 (0.86–1.86)	0.23
AA/AD status			
No lifetime AUD	53.2	Reference	
Remitted AA	51.3	0.94 (0.63–1.40)	0.75
Current AA	45.7	0.79 (0.43–1.45)	0.45
Remitted AD	62.4	1.42 (1.02–1.97)	0.04
Current AD	66.7	1.69 (1.04–2.75)	0.04
AD severity			
No lifetime AUD	53.2	Reference	
Moderate current AD (3–5 criteria)	57.4	1.11 (0.65–1.89)	0.69
Severe current AD (6 or 7 criteria)	95.0	17.15 (2.27–129.51)	0.006

AA, alcohol abuse; AD, alcohol dependence; AUD, alcohol use disorder; OR, odds ratio.

a. Based on logistic regression analyses, adjusted for basic covariates (gender, age and smoking status).

increased risk of having a persistent depressive and/or anxiety disorder at the 2-year follow-up compared with participants with no lifetime alcohol use disorder (persistence: 53.2%). In contrast, neither remitted nor current alcohol abuse significantly predicted the presence of depressive and/or anxiety disorders after 2 years.

**Fig. 1** Alcohol abuse and dependence status predicting the course of (a) depressive symptoms and (b) anxiety symptoms.

Based on linear mixed model analyses, adjusted for basic covariates (gender, age and smoking status). Probability values are given in Table 3. AA, alcohol abuse; AD, alcohol dependence; AUD, alcohol use disorder; BAI, Beck Anxiety Inventory; IDS, Inventory of Depressive Symptomatology.

We tested the robustness of these findings with LMM analyses adjusted for basic covariates (Fig. 1). Over the entire follow-up period, participants with remitted and current alcohol dependence had significantly higher overall levels of depressive symptoms and a trend was found for anxiety symptoms (see Table 3 for probability values), with similar course trajectories over time ($P \geq 0.10$ for all interactions remitted dependence \times time or current dependence \times time), compared with participants with no lifetime alcohol use disorder. Neither the overall levels nor the course trajectories of depressive and anxiety symptoms were significantly worse for people with remitted or current alcohol abuse.

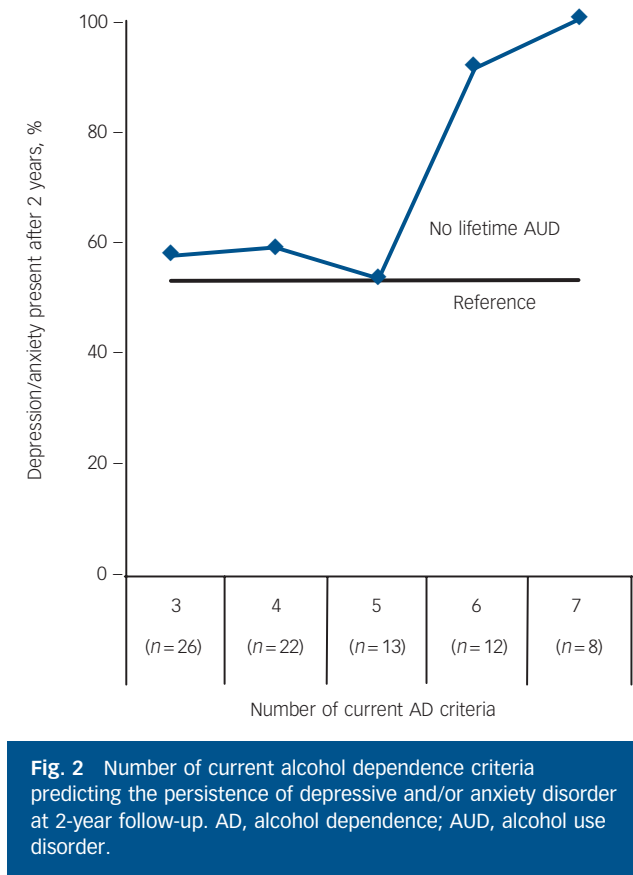
Severity of alcohol abuse and dependence

A third aim of our study was to examine whether the associations of current alcohol abuse and dependence with the course of depressive and/or anxiety disorders were conditional on the severity of each condition. Analyses of alcohol abuse severity appeared to be impossible, since of the 46 participants in the current alcohol abuse group, 44 met only one DSM-IV abuse criterion (see Table 1), so further analyses were restricted to the severity of current alcohol dependence. A graph of the association between the number of current alcohol dependence criteria and the presence of depressive and/or anxiety disorders at the 2-year follow-up (Fig. 2) indicated that this association was conditional on the severity of dependence. Only people meeting six or seven alcohol dependence criteria, and not those meeting three, four or five criteria, were at an increased risk. To test this directly, we

Table 3 Probability values for prediction of course of symptoms by alcohol abuse and dependence status (see Fig. 1)

	Depressive symptoms		Anxiety symptoms	
	Direct effect <i>P</i>	Time interaction <i>P</i>	Direct effect <i>P</i>	Time interaction <i>P</i>
Remitted AA	0.80	0.91	0.70	0.26
Current AA	0.03	0.25	0.02	0.24
Remitted AD	0.02	0.91	0.07	0.67
Current AD	0.04	0.54	0.18	0.10

AA, alcohol abuse; AD, alcohol dependence.



used a model distinguishing no lifetime alcohol use disorder, ‘moderate’ current alcohol dependence (meeting three to five criteria) and ‘severe’ current alcohol dependence (six or seven criteria). This two-level model explained the relationship with the persistence of depressive and/or anxiety disorders better than the original DSM-IV model which made no distinction based on severity of alcohol dependence ($\chi^2 = 7.10$, d.f. = 1, $P = 0.008$). Additional analyses, taking moderate alcohol dependence as the reference group, showed a significant difference between people with severe alcohol dependence and those with moderate dependence (unadjusted OR = 14.11, 95% CI 1.77–112.29, $P = 0.01$), indicating that severe alcohol dependence had a significantly stronger effect on the persistence of depressive and/or anxiety disorders.

Table 2 shows that 95.0% of participants with severe alcohol dependence still had a depressive and/or anxiety disorder after the 2-year follow-up, which was significantly higher than in those with no lifetime alcohol use disorder (basic adjustment: OR = 17.15, 95% CI 2.27–129.51, $P = 0.006$). No significant association was found for participants with moderate alcohol

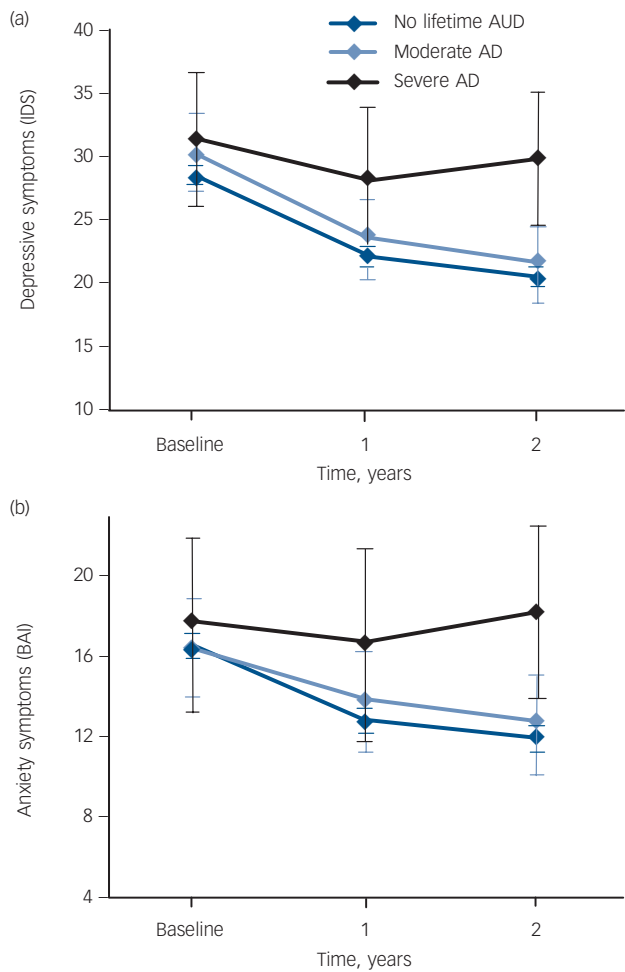


Fig. 3 Moderate and severe current alcohol dependence predicting the course of (a) depressive symptoms and (b) anxiety symptoms.

Based on linear mixed model analyses, adjusted for basic covariates (gender, age, and smoking status). Probability values are given in Table 4. AD, alcohol dependence; AUD, alcohol use disorder; BAI, Beck Anxiety Inventory; IDS, Inventory of Depressive Symptomatology.

dependence (basic adjustment: OR = 1.11, 95% CI 0.65–1.89, $P = 0.69$). To verify our findings regarding the persistence of depressive and/or anxiety disorders at 2 years follow-up, we additionally tested whether moderate alcohol dependence and severe alcohol dependence predicted the course of depressive and anxiety symptoms using LMM analyses (Fig. 3). These results showed that the overall levels of depressive and anxiety symptoms were higher for those with severe current alcohol dependence and that, in addition, the course trajectories for depressive and anxiety symptoms were poorer compared with those with no lifetime

	Depressive symptoms		Anxiety symptoms	
	Direct effect <i>P</i>	Time interaction <i>P</i>	Direct effect <i>P</i>	Time interaction <i>P</i>
Moderate current AD (3–5 criteria)	0.33	0.89	0.63	0.61
Severe current AD (6 or 7 criteria)	0.01	0.02	0.06	0.02

AD, alcohol dependence.

alcohol use disorder (P values are summarised in Table 4). No significant difference in the course of depressive or anxiety symptoms was found for moderate alcohol dependence.

Role of other factors

To explore the role of other factors in the association between severity of alcohol dependence and the persistence of depressive and/or anxiety disorders, the analyses were additionally adjusted for baseline severity of depression and anxiety (Table 5, second column), psychosocial factors (third column) and treatment factors (fourth column). In the analyses adjusted for basic covariates, severe current alcohol dependence was a significant predictor of the persistence of depressive and/or anxiety disorders (OR = 17.15, 95% CI 2.27–129.51, $P=0.006$). Although the association was slightly decreased after additional adjustment for severity of depressive and anxiety symptoms (OR = 15.88, 95% CI 2.09–120.87, $P=0.008$), psychosocial factors (OR = 15.22, 95% CI 1.99–116.16, $P=0.009$) and treatment factors (OR = 13.50, 95% CI 1.77–102.96, $P=0.01$), the association remained significant (Table 5).

Heterogeneity of depressive and anxiety disorders

At the baseline assessment, 60.4% of all the participants who had current depression also had a current anxiety disorder. Similarly, 57.4% of participants with current anxiety also had a current depressive disorder. Given the high comorbidity of depressive and anxiety disorders, previous analyses were based on a mixed group of people with a depressive and/or anxiety disorder. To assess the robustness of our findings, a set of sensitivity analyses was conducted. First, we tested whether alcohol abuse/dependence status predicted the presence of a depressive and/or anxiety

disorder at the 2-year follow-up in a subsample of participants with depressive disorders ($n=946$) *v.* those with anxiety disorders ($n=994$). We found consistent associations for remitted alcohol abuse (unadjusted OR = 0.69, $P=0.12$ *v.* unadjusted OR = 1.06, $P=0.80$), current alcohol abuse (unadjusted OR = 0.58, $P=0.14$ *v.* unadjusted OR = 0.74, $P=0.43$), remitted alcohol dependence (unadjusted OR = 1.26, $P=0.25$ *v.* unadjusted OR = 1.67, $P=0.04$) and current alcohol dependence (unadjusted OR = 1.47, $P=0.16$ *v.* unadjusted OR = 1.75, $P=0.05$). In addition, severe current alcohol dependence was a significant predictor in participants with depressive disorders (unadjusted OR = 11.26, $P=0.02$) and anxiety disorders (unadjusted OR = 10.29, $P=0.03$), whereas moderate current alcohol dependence was not significant in either subsample (unadjusted OR = 0.99, $P=0.96$ *v.* unadjusted OR = 1.28, $P=0.43$).

Discussion

To our knowledge this is the first study showing that the association between alcohol use disorders and the course of depressive and/or anxiety disorders is conditional on the type (abuse or dependence) and severity of the alcohol use disorder. Our results show that current dependence as well as a history of alcohol dependence, but not abuse, predicts an unfavourable course of depressive and/or anxiety disorders. People with severe current alcohol dependence (six or seven alcohol dependence criteria) have an especially poor course since 95% have a persistent depressive and/or anxiety disorder, in contrast to 53% of those with no lifetime alcohol use disorder. In addition, depressive and anxiety symptoms remain significantly higher in people with severe current alcohol dependence, whereas they generally

Table 5 Alcohol use disorder measures predicting the persistence of depressive and/or anxiety disorders at 2-year follow-up

	Persistence of depressive/anxiety disorder after 2 years							
	Basic adjustment ^a		Additionally adjusted for symptom severity ^b		Additionally adjusted for psychosocial factors ^c		Additionally adjusted for treatment factors ^d	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
AD severity								
No lifetime AUD	Reference		Reference		Reference		Reference	
Moderate current AD	1.11 (0.65–1.89)	0.71	1.03 (0.59–1.80)	0.92	1.00 (0.57–1.75)	1.00	0.97 (0.55–1.72)	0.93
Severe current AD	17.15 (2.27–129.51)	0.006	15.88 (2.09–120.87)	0.008	15.22 (1.99–116.16)	0.009	13.50 (1.77–102.96)	0.01
Basic covariates								
Gender (female)	1.11 (0.83–1.48)	0.49	1.13 (0.83–1.53)	0.43	1.12 (0.83–1.52)	0.46	1.12 (0.82–1.52)	0.48
Age	1.01 (1.00–1.02)	0.01	1.01 (1.00–1.02)	0.08	1.01 (1.00–1.02)	0.08	1.01 (1.00–1.03)	0.02
Smoking status								
Non-smoker	Reference		Reference		Reference		Reference	
Former smoker	1.36 (0.98–1.88)	0.06	1.21 (0.86–1.70)	0.27	1.19 (0.84–1.67)	0.33	1.17 (0.83–1.65)	0.37
Current smoker	1.65 (1.21–2.25)	0.002	1.43 (1.03–1.98)	0.03	1.42 (1.02–1.98)	0.04	1.43 (1.02–1.99)	0.04
Severity of depression and anxiety								
Depressive symptoms (IDS score)			1.05 (1.04–1.07)	<0.001	1.05 (1.03–1.07)	<0.001	1.05 (1.03–1.06)	<0.001
Anxiety symptoms (BAI score)			1.01 (0.99–1.02)	0.37	1.01 (0.99–1.03)	0.32	1.01 (0.99–1.02)	0.38
Psychosocial factors								
Education in years					1.01 (0.97–1.06)	0.53	1.00 (0.96–1.05)	0.84
Employment (yes)					0.90 (0.69–1.18)	0.46	0.91 (0.69–1.20)	0.51
Partner (yes)					0.91 (0.69–1.21)	0.53	0.91 (0.68–1.21)	0.51
Treatment factors								
Use of antidepressants (yes)							1.00 (0.76–1.32)	1.00
Use of benzodiazepines (yes)							0.91 (0.64–1.30)	0.62
Psychological treatment (yes)							1.63 (1.20–2.20)	0.002

AD, alcohol dependence; AUD, alcohol use disorder; BAI, Beck Anxiety Inventory; IDS, Inventory of Depressive Symptomatology; OR, odds ratio.

a. Adjusted for basic covariates (gender, age, smoking status).

b. Adjusted for basic covariates and depressive/anxiety symptoms (baseline IDS and BAI scores).

c. Adjusted for basic covariates, depressive/anxiety symptoms and psychosocial factors (education, employment status, partner status).

d. Adjusted for basic covariates, depressive/anxiety symptoms, psychosocial factors and treatment factors (use of antidepressants, use of benzodiazepines and psychological treatment).

improve in those with no lifetime alcohol use disorder. The inconsistent findings of previous studies reporting that alcohol use disorders predicted an unfavourable course of depressive or anxiety disorders,^{16,17} or did not,^{11,18} may therefore be explained by the differential effects of alcohol use disorders depending on the type and severity.

Possible mechanisms

Our study further demonstrated that severe current alcohol dependence predicted the persistence of depressive and/or anxiety disorders, even after taking into account the effects of other risk factors. Although baseline severity of depressive and anxiety symptoms, psychosocial factors and treatment partly explained the association, severe alcohol dependence remained a strong predictor. Previous studies have proposed that interpersonal and social problems, as characteristics of alcohol use disorders, cause the persistence of depressive and/or anxiety disorders.³² This may be supported by our finding that the risk of persistent depressive and/or anxiety disorders was increased only in people with severe alcohol dependence. Previous studies have found that the alcohol dependence criterion involving interpersonal and social problems (criterion 6: giving up or reducing occupational, social and/or recreational activities to drink) is one of the most severe criteria and is mainly present in those with severe alcohol use disorders.³³ This was supported by some additional analyses showing that this specific criterion was present in 85% of participants with severe alcohol dependence *v.* 15% of those with moderate alcohol dependence. Similarly, DSM-IV alcohol abuse criteria involving interpersonal and social problems (criterion 1: failure to fulfil major role obligations; criterion 4: persistent social or interpersonal problems) are more likely in people with severe alcohol use disorders;³⁴ the prevalence rates of alcohol abuse criteria 1 and 4 in participants with severe alcohol dependence in our sample were 60% and 100% respectively. Although factors involving general psychosocial status (level of education, employment status and partner status) did not explain the association between severe current alcohol dependence and the persistence of depressive and/or anxiety disorders, factors involving the quality of interpersonal and social life (giving up activities, failure to fulfil roles, and persistent social or interpersonal problems), as characteristics of severe alcohol dependence, may have a more important role. Further research is needed to unravel the exact mechanisms through which (severe) current alcohol dependence leads to an unfavourable course of depressive and/or anxiety disorders.

Clinical implications

Our finding that (severe) current alcohol dependence leads to an unfavourable course of depressive and/or anxiety disorders stresses the importance of integrating addiction treatment in general mental health services to optimise treatment for patients with depression and/or anxiety with comorbid alcohol dependence. This has the potential to be highly effective, since 95% of our sample with severe current alcohol dependence had a persistent depressive and/or anxiety disorder after 2 years. Integrated care has also been advocated by others as a means of enhancing communication between care providers, reducing stigma and avoiding artificial separation of various psychiatric problems that otherwise could result in substandard care.^{34,35} To identify individuals with alcohol dependence, time-efficient screening instruments such as the Alcohol Use Disorder Identification Test (AUDIT) could be helpful.³⁶ This test has been shown to be accurate in detecting alcohol dependence in individuals with depression and anxiety,³⁷ and therefore may be effective in

identifying patients with depression and/or anxiety who need additional addiction treatment.

Alcohol use disorder in DSM-5

We showed that alcohol abuse, unlike dependence, does not predict the course of depressive and/or anxiety disorders. A similar pattern of results was found in other studies reporting that alcohol abuse was not more prevalent in people with anxiety and/or depression, in contrast to dependence.^{14,15} Since others found that the reliability and validity were excellent for a DSM-IV diagnosis of alcohol dependence but not for a diagnosis of alcohol abuse,^{29,36} this raises the question whether alcohol abuse as diagnosed by DSM-IV criteria (*i.e.* hierarchically assessed based on one or more criteria) should be considered a genuine psychiatric disorder. This may be supported by our finding that of the 46 persons with current alcohol abuse in our sample, all but 2 met only one criterion. Although the reliability and validity of a diagnosis of alcohol abuse were low, studies have shown that the individual criteria of alcohol dependence as well as abuse are reliable and valid, and represent a single latent dimension with dependence and abuse criteria interspersed across an underlying severity spectrum.^{37–39} Together, these findings have motivated the DSM-5 work group to propose one diagnosis of an alcohol use disorder that is based on alcohol abuse as well as dependence criteria, with different levels of severity. The importance of using severity indicators rather than categorical diagnoses is also highlighted by our finding that only those with severe alcohol dependence (meeting six or seven criteria) and not those with moderate alcohol dependence (meeting three to five criteria) have an unfavourable course of depressive and/or anxiety disorders. Severity of disorder may therefore be more informative than pure diagnosis, as has already been indicated by others.^{37–41}

Strengths and limitations

Methodological strengths of our study include that we prospectively examined whether DSM-IV alcohol abuse and alcohol dependence predicted the course of disorders in a large sample of people with a DSM-IV diagnosis of a depressive and/or anxiety disorder. This sample consisting of 1369 persons was much larger than the 92 to 588 persons who participated in previous studies on this topic.^{11,16–18} In addition, our main findings regarding the persistence of depressive and/or anxiety disorders were all supported by additional analyses on the course of depressive and anxiety symptoms. Despite the large sample size, a limitation of our study is the small number of participants with severe alcohol use disorders. In addition, people with a primary diagnosis of a severe substance use disorder were not included in this study. Therefore, reported associations between alcohol use disorders and the course of depressive and/or anxiety disorders are likely to be underestimates and may not be generalised to severe alcohol use disorders. Studies in clinical samples of patients with severe alcohol use disorders, with or without comorbid substance use disorders, should provide important additional information. Although consistent findings were found for participants with a depressive disorder *v.* an anxiety disorder, further research is needed to assess associations between alcohol use disorders and specific depressive and anxiety disorders.

Concluding remarks

The effects of comorbid alcohol use disorders on the course of depressive and/or anxiety disorders are conditional on the type as well as severity of the former disorders. Alcohol dependence,

especially severe current dependence, predicts an unfavourable course of depressive and/or anxiety disorders, whereas alcohol abuse does not. Of the group with severe current alcohol dependence, 95% had a persistent depressive and/or anxiety disorder without symptomatic improvement. This stresses the importance of integrating addiction treatment in general mental health services as a means of optimising treatment outcomes for patients with depression and/or anxiety.

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First received 3 Jun 2011, final revision 17 Aug 2011, accepted 26 Oct 2011

Funding

The infrastructure for The Netherlands Study of Depression and Anxiety (<http://www.nesda.nl>) is funded through the Geestkracht programme of The Netherlands Organisation for Health Research and Development (Zon-Mw, grant number 10-000-1002) and is supported by participating universities and mental healthcare organisations: VU University Medical Centre, GGZ inGeest, Arkin, Leiden University Medical Centre, GGZ Rivierduinen, University Medical Centre Groningen, Lentis, GGZ Friesland, GGZ Drenthe, Scientific Institute for Quality of Health Care (IQ Healthcare), Netherlands Institute for Health Services Research (NIVEL) and Netherlands Institute of Mental Health and Addiction (Trimbos). Data analyses were supported by grant 31160004 from The Netherlands Organisation for Health Research and Development.

References

- Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry* 1994; **51**: 8–19.
- Judd LL, Akiskal HS, Zeller PJ, Paulus M, Leon AC, Maser JD, et al. Psychosocial disability during the long-term course of unipolar major depressive disorder. *Arch Gen Psychiatry* 2000; **57**: 375–80.
- World Health Organization. *The World Health Report 2001: Mental Health: New Understanding, New Hope*. WHO, 2001.
- World Health Organization. *The World Health Report 2003: Shaping the Future*. WHO, 2003.
- Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006; **367**: 1747–57.
- Ormel J, Petukhova M, Chatterji S, Aguilar-Gaxiola S, Alonso J, Angermeyer MC, et al. Disability and treatment of specific mental and physical disorders across the world. *Br J Psychiatry* 2008; **192**: 368–75.
- Piccinelli M, Wilkinson G. Outcome of depression in psychiatric settings. *Br J Psychiatry* 1994; **164**: 297–304.
- Pollack MH, Otto MW. Long-term course and outcome of panic disorder. *J Clin Psychiatry* 1997; **58**: 57–60.
- Judd LL, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, et al. A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. *Arch Gen Psychiatry* 1998; **55**: 694–700.
- Keller MB. Social anxiety disorder clinical course and outcome: Review of Harvard/Brown Anxiety Research Project (HARP) findings. *J Clin Psychiatry* 2006; **67**: 14–9.
- Rhebergen D, Beekman ATF, De Graaf R, Nolen WA, Spijker J, Hoogendijk WJ, et al. The three-year naturalistic course of major depressive disorder, dysthymic disorder and double depression. *J Affect Disord* 2009; **115**: 450–9.
- Burns L, Teesson M. Alcohol use disorders comorbid with anxiety, depression and drug use disorders. Findings from the Australian National Survey of Mental Health and Well Being. *Drug Alcohol Depend* 2002; **68**: 299–307.
- De Graaf R, Bijl RV, Smit F, Vollebergh WA, Spijker J. Risk factors for 12-month comorbidity of mood, anxiety, and substance use disorders: findings from the Netherlands Mental Health Survey and Incidence Study. *Am J Psychiatry* 2002; **159**: 620–9.
- Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry* 2007; **64**: 830–42.
- Boschloo L, Vogelzangs N, Smit JH, Van den Brink W, Veltman DJ, Beekman AT, et al. Comorbidity and risk indicators for alcohol use disorders among persons with anxiety and/or depressive disorders: findings from the Netherlands Study of Depression and Anxiety (NESDA). *J Affect Disord* 2011; **131**: 233–42.
- Mueller TI, Lavori PW, Keller MB, Swartz A, Warshaw M, Hasin D, et al. Prognostic effect of the variable course of alcoholism on the 10-year course of depression. *Am J Psychiatry* 1994; **151**: 701–6.
- Bruce SE, Yonkers KA, Otto MW, Eisen JL, Weisberg RB, Pagano M, et al. Influence of psychiatry comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: a 12-year prospective study. *Am J Psychiatry* 2005; **162**: 1179–87.
- Kushner MG, Sher KJ, Erickson DJ. Prospective analysis of the relation between DSM-III anxiety disorders and alcohol use disorders. *Am J Psychiatry* 1999; **156**: 723–32.
- Muthen BO, Hasin DS, Wisnicki KS. Factor analysis of ICD-10 symptom items in the 1988 National Health Interview Survey. *Addiction* 1993; **88**: 1071–7.
- Harford TC, Muthen BO. The dimensionality of alcohol abuse and dependence: a multivariate analysis of DSM-IV symptom items in the National Longitudinal Survey of Youth. *Drug Alcohol Depend* 2001; **62**: 150–7.
- Hasin DS, Liu X, Alderson D, Grant BF. DSM-IV alcohol dependence: a categorical or dimensional phenotype. *Psychol Med* 2006; **36**: 1695–705.
- Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SL, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychol Med* 2002; **32**: 959–76.
- Wittchen HU, Robins LN, Cottler LB, Sartorius N, Burke JD, Regier D. Cross-cultural feasibility, reliability and sources of variance of the Composite International Diagnostic Interview (CIDI). The Multicentre WHO/ADAMHA Field Trials. *Br J Psychiatry* 1991; **159**: 645–53, 658.
- Penninx BW, Beekman AT, Smit JH, Zitman FG, Nolen WA, Spinhoven P, et al. The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *Int J Methods Psychiatr Res* 2008; **17**: 121–40.
- Van der Veen WJ, Van der Meer K, Penninx BW. Screening for depression and anxiety: correlates of non-response and cohort attrition in the Netherlands Study of Depression and Anxiety (NESDA). *Int J Methods Psychiatr Res* 2009; **18**: 229–39.
- Lamers F, Hoogendoorn A, Smit J, Van Dyck R, Zitman FG, Nolen WA, et al. Sociodemographic and psychiatric determinants of attrition in the Netherlands Study of Depression and Anxiety (NESDA). *Compr Psychiatry* 2011; **53**: 63–70.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders* (4th edn) (DSM-IV). APA, 1994.
- Rush AJ, Gullion CM, Basco MR, Jarret RB, Trivedi MH. The Inventory of Depressive Symptomatology (IDS): psychometric properties. *Psychol Med* 1996; **26**: 477–86.
- Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol* 1988; **56**: 893–7.
- Cottler LB, Grant BF, Blaine J, Mavreas V, Pull C, Hasin D, et al. Concordance of DSM-IV alcohol and drug use disorder criteria and diagnoses as measured by AUDADIS-ADR, CIDI and SCAN. *Drug Alcohol Depend* 1997; **47**: 195–205.
- World Health Organization Collaborating Centre for Drug Statistics Methodology. *Anatomical Therapeutic Chemical (ATC) Classification*. WHO, 2007.
- Swendsen JD, Merikangas KR. The comorbidity of depression and substance use disorders. *Clin Psychol Rev* 2000; **20**: 173–89.
- Dawson DA, Saha TD, Grant BF. A multidimensional assessment of the validity and utility of alcohol use disorder severity as determined by item response theory models. *Drug Alcohol Depend* 2010; **107**: 31–8.
- Mechanic D. Approaches for coordinating primary and specialty care for persons with mental illness. *Gen Hosp Psychiatry* 1997; **19**: 395–402.

- 35 Bartels SJ, Coakley EH, Zubritsky C, Ware JH, Miles KM, Areán PA, et al. Improving access to geriatric mental health services: a randomized trial comparing treatment engagement with integrated versus enhanced referral care for depression, anxiety, and at-risk alcohol use. *Am J Psychiatry* 2004; **161**: 1455–62.
- 36 Saunders JB, Aasland OF, Babor TF, Fuente JRD, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on early detection of persons with harmful alcohol consumption – II. *Addiction* 1993; **88**: 791–804.
- 37 Boschloo L, Vogelzangs N, Smit JH, Van den Brink W, Veltman DJ, Beekman ATF, et al. The performance of the Alcohol Use Disorder Identification Test (AUDIT) in detecting alcohol abuse and alcohol dependence in a population of depressed or anxious persons. *J Affect Disord* 2010; **126**: 441–6.
- 38 Hasin DS, Schuckit MA, Martin CS, Grant BF, Bucholz KK, Helzer JE. The validity of DSM-IV alcohol dependence: what do we know and what do we need to know? *Alcohol Clin Exp Res* 2003; **27**: 244–52.
- 39 Saha TD, Chou SP, Grant BF. Toward an alcohol use disorder continuum using item response theory: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychol Med* 2006; **36**: 931–41.
- 40 Hasin DS, Beseler CL. Dimensionality of lifetime alcohol abuse, dependence and binge drinking. *Drug Alcohol Depend* 2009; **101**: 53–61.
- 41 Boschloo L, Van den Brink W, Penninx BWJH, Wall MM, Hasin DS. Alcohol-use disorder severity predicts first-incidence of depressive disorders. *Psychol Med* 2011; Aug 26; doi:10.1017/S0033291711001681. Epub ahead of print.

poem

Cancer Winter (excerpts)

Marilyn Hacker

I woke up, and the surgeon said, 'You're cured.'
 Strapped to the gurney, in the cotton gown
 and pants I was wearing when they slid me down
 onto the table, made news straps secure
 while I stared at the hydra-headed O.R.
 lamp, I took in the tall, confident, brown-
 skinned man, and the ache I couldn't quite call pain
 from where my right breast wasn't anymore
 to my armpit. A not-yet-talking head,
 I bit dry my lips. What else could he have said?
 And then my love was there in a hospital coat;
 then my old love, still young and very scared.
 Then I, alone, graphed clock hands' asymptote
 to noon, when I would be wheeled back upstairs.
 (. . .)
 The hand that held the cup next was my daughter's
 – who would be holding shirts for me to wear,
 sleeve out, for my bum arm. She'd wash my hair
 (not falling yet), strew teenager's disorder
 in the kitchen, help me out of the bathwater.
 A dozen times, she looked at the long scar
 studded with staples, where I'd suckled her,
 and didn't turn. She took me / I brought her
 to the surgeon's office, where she'd hold
 my hand, while his sure hand, with its neat tool, snipped
 the steel, as on a revised manuscript
 radically rewritten since my star
 turn nursing her without a 'nursing bra'
 from small, firm breasts, a twenty-five-year-old's.

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Chosen by Femi Oyeboode.

The British Journal of Psychiatry (2012)
 200, 484. doi: 10.1192/bjp.bp.112.112532